

1/10

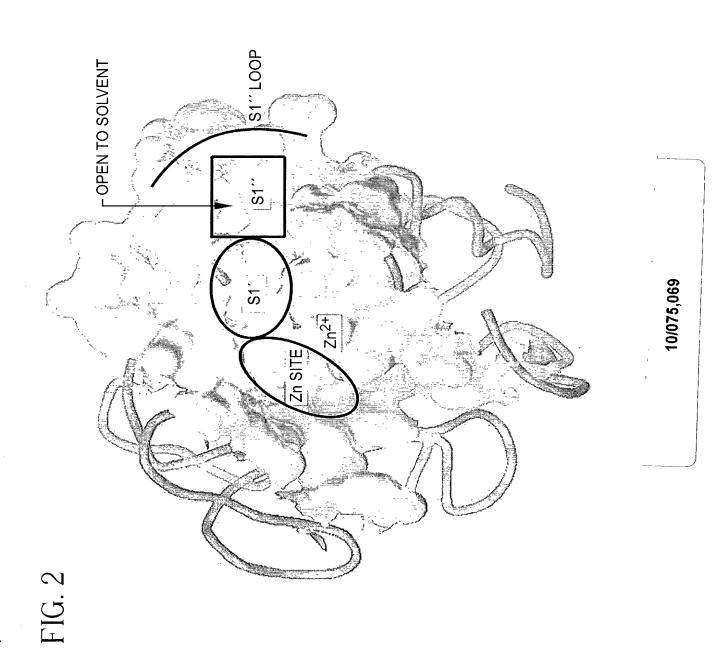
## FIG. 1

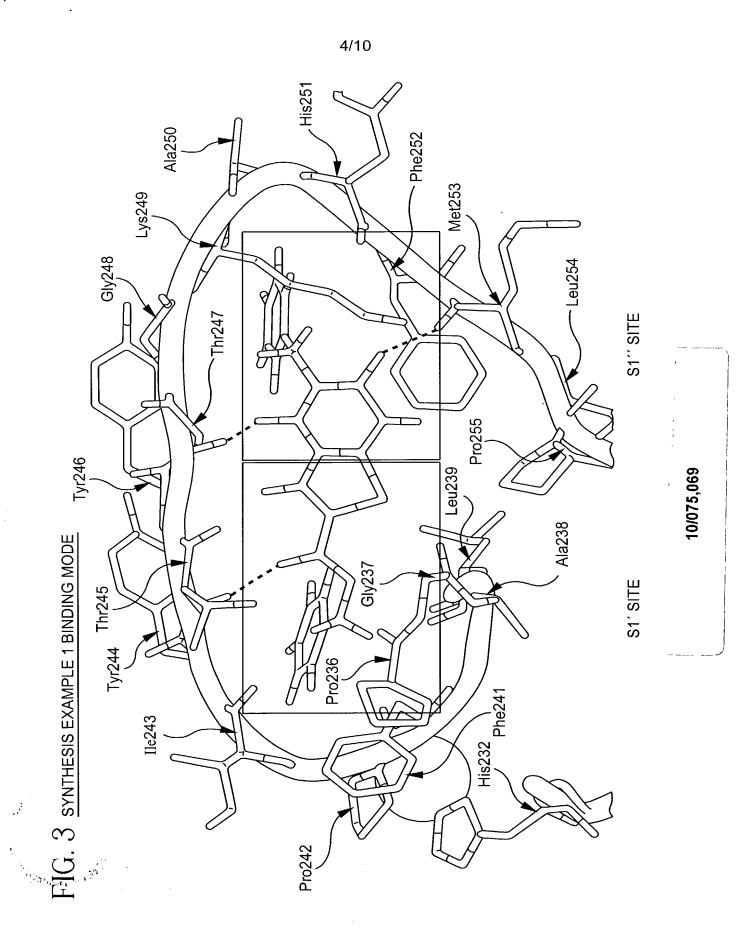
|          | SEQUENCE LISTING  |             |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
|----------|---|-------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| 5        | <110> WARNER-LAMBERT                                    |             |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
|          | <120> Matrix metalloproteinase inhibitors               |             |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
| 10       | <130> A0000434  |             |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
|          | <140><br><141>  |             |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
| 15       | <160> 1   |             |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
|          | <170> PatentIn Ver. 2.1                                 |             |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
| 20       | <210> 1<br><211> 471<br><212> PRT<br><213> Homo sapiens |             |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
| 25       | <400<br>Met<br>1  | )> 1<br>His | Pro        | Gly        | Val<br>5   | Leu        | Ala        | Ala        | Phe        | Leu<br>10  | Phe        | Leu        | Ser        | Trp        | Thr<br>15  | His        |
|          | Cys   | Arg         | Ala        | Leu<br>20  | Pro        | Leu        | Pro        | Ser        | Gly<br>25  | Gly        | Asp        | Glu        | Asp        | Asp<br>30  | Leu        | Ser        |
| 30       | Glu   | Glu         | Asp<br>35  | Leu        | Gln        | Phe        | Ala        | Glu<br>40  | Arg        | Tyr        | Leu        | Arg        | Ser<br>45  | Tyr        | Tyr        | His        |
|          | Pro   | Thr<br>50   | Asn        | Leu        | Ala        | Gly        | Ile<br>55  | Leu        | Lys        | Glu        | Asn        | Ala<br>60  | Ala        | Ser        | Ser        | Met        |
| 35       | Thr<br>65   | Glu         | Arg        | Leu        | Arg        | Glu<br>70  | Met        | Gln        | Ser        | Phe        | Phe<br>75  | Gly        | Leu        | Glu        | Val        | Thr<br>80  |
| 40       | Gly   | Lys         | Leu        | Asp        | Asp<br>85  | Asn        | Thr        | Leu        | Asp        | Val<br>90  | Met        | Lys        | Lys        | Pro        | Arg<br>95  | Cys        |
|          | Gly   | Val         | Pro        | Asp<br>100 | Val        | Gly        | Glu        | Tyr        | Asn<br>105 | Val        | Phe        | Pro        | Arg        | Thr<br>110 | Leu        | Lys        |
| 45       | Trp   | Ser         | Lys<br>115 | Met        | Asn        | Leu        | Thr        | Tyr<br>120 | Arg        | Ile        | Val        | Asn        | Tyr<br>125 | Thr        | Pro        | Asp        |
|          | Met   | Thr<br>130  | His        | Ser        | Glu        | Val        | Glu<br>135 | Lys        | Ala        | Phe        | Lys        | Lys<br>140 | Ala        | Phe        | Lys        | Val        |
| 50       | Trp<br>.145   | Ser         | Asp        | Val        | Thr        | Pro<br>150 | Leu        | Asn        | Phe        | Thr        | Arg<br>155 | Leu        | His        | Asp        | Gly        | Ile<br>160 |
| 55       | Ala   | Asp         | Ile        | Met        | Ile<br>165 | Ser        | Phe        | Gly        | Ile        | Lys<br>170 | Glu        | His        | Gly        | Asp        | Phe<br>175 | Tyr        |
| on and a | 3.5   | Phe         | Asp        | Gly<br>180 | Pro        | Ser        | Gly        | Leu        | Leu<br>185 | Ala        | His        | Ala        | Phe        | Pro<br>190 | Pro        | Gly        |

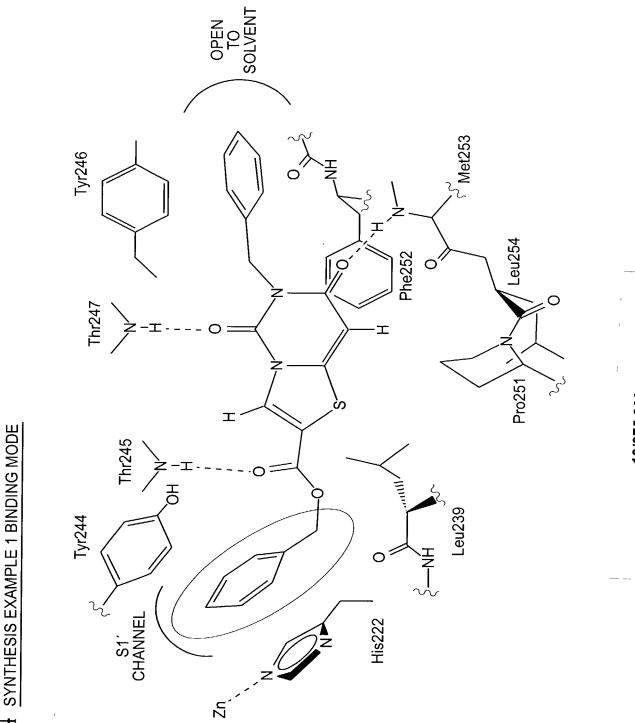
## 2/10

## FIG. 1A

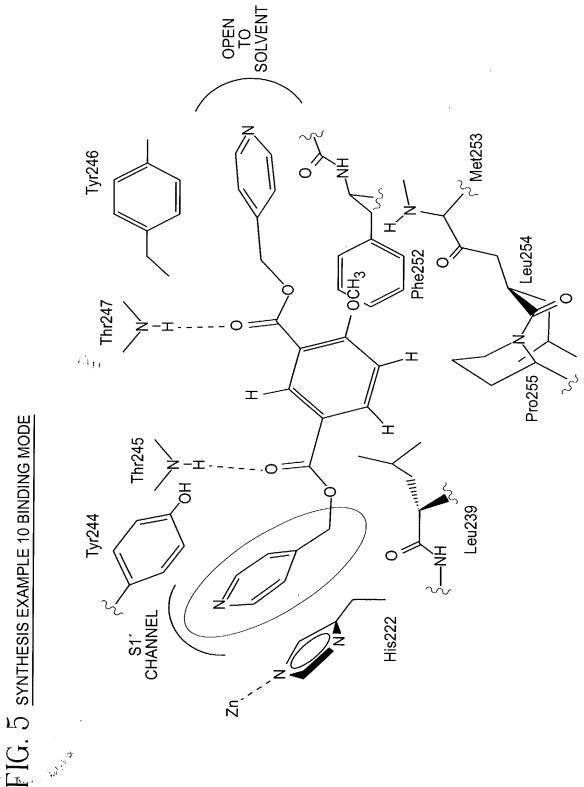
| _      | Pro        | o Ası      | 195        | Tyr Gly Gly Asp Ala<br>195 |            |            |            |            | s Phe      | e Asp      | p Ası      | Asp Glu Thr Trp Thi<br>205 |            |            |            |            |
|--------|------------|------------|------------|----------------------------|------------|------------|------------|------------|------------|------------|------------|----------------------------|------------|------------|------------|------------|
| 5      | Ser        | Ser<br>210 | Ser        | Lys                        | Gly        | Tyr        | Asn<br>215 | Leu        | Phe        | Leu        | Val        | Ala<br>220                 | Ala        | His        | Glu        | Phe        |
| 10     | Gly<br>225 | His        | Ser        | Leu                        | Gly        | Leu<br>230 | Asp        | His        | Ser        | Lys        | Asp<br>235 | Pro                        | Gly        | Ala        | Leu        | Met<br>240 |
|        | Phe        | Pro        | Ile        | Tyr                        | Thr<br>245 | Tyr        | Thr        | Gly        | Lys        | Ser<br>250 | His        | Phe                        | Met        | Leu        | Pro<br>255 | Asp        |
| 15     | Asp        | Asp        | Val        | Gln<br>260                 | Gly        | Ile        | Gln        | Ser        | Leu<br>265 | Tyr        | Gly        | Pro                        | Gly        | Asp<br>270 | Glu        | Asp        |
| 20     | Pro        | Asn        | Pro<br>275 | Lys                        | His        | Pro        | Lys        | Thr<br>280 | Pro        | Asp        | Lys        | Cys                        | Asp<br>285 | Pro        | Ser        | Leu        |
|        | Ser        | Leu<br>290 | Asp        | Ala                        | Ile        | Thr        | Ser<br>295 | Leu        | Arg        | Gly        | Glu        | Thr<br>300                 | Met        | Ile        | Phe        | Lys        |
| 25     | Asp<br>305 | Arg        | Phe        | Phe                        | Trp        | Arg<br>310 | Leu        | His        | Pro        | Gln        | Gln<br>315 | Val                        | Asp        | Ala        | Glu        | Leu<br>320 |
|        | Phe        | Leu        | Thr        | Lys                        | Ser<br>325 | Phe        | Trp        | Pro        | Glu        | Leu<br>330 | Pro        | Asn                        | Arg        | Ile        | Asp<br>335 | Ala        |
| 30     | Ala        | Tyr        | Glu        | His<br>340                 | Pro        | Ser        | His        | Asp        | Leu<br>345 | Ile        | Phe        | Ile                        | Phe        | Arg<br>350 | Gly        | Arg        |
| 35     | Lys        | Phe        | Trp<br>355 | Ala                        | Leu        | Asn        | Gly        | Tyr<br>360 | Asp        | Ile        | Leu        | Glu                        | Gly<br>365 | Tyr        | Pro        | Lys        |
|        | Lys        | Ile<br>370 | Ser        | Glu                        | Leu        | Gly        | Leu<br>375 | Pro        | Lys        | Glu        | Val        | Lys<br>380                 | Lys        | Ile        | Ser        | Ala        |
| 40     | Ala<br>385 | Val        | His        | Phe                        | Glu        | Asp<br>390 | Thr        | Gly        | Lys        | Thr        | Leu<br>395 | Leu                        | Phe        | Ser        | Gly        | Asn<br>400 |
|        | Gln        | Val        | Trp        | Arg                        | Tyr<br>405 | Asp        | Asp        | Thr        | Asn        | His<br>410 | Ile        | Met                        | Asp        | Lys        | Asp<br>415 | Tyr        |
| 45     | Pro        | Arg        | Leu        | Ile<br>420                 | Glu        | Glu        | Asp        | Phe        | Pro<br>425 | Gly        | Ile        | Gly                        | Asp        | Lys<br>430 | Val        | Asp        |
| <br>50 | Ala        | Val        | Tyr<br>435 | Glu                        | Lys        | Asn        | Gly        | Tyr<br>440 | Ile        | Tyr        | Phe        | Phe                        | Asn<br>445 | Gly        | Pro        | Ile        |
|        | Gln        | Phe<br>450 | Glu        | Tyr                        | Ser        | Ile        | Trp<br>455 | Ser        | Asn        | Arg        | Ile        | Val<br>460                 | Arg        | Val        | Met        | Pro        |
| 55 :   |            | Asn        | Ser        | Ile                        | Leu        | Trp        | Cys        |            |            |            |            |                            |            |            |            |            |







G. 4 SYNTHESIS EXAMPLE 1 BINDING MODE



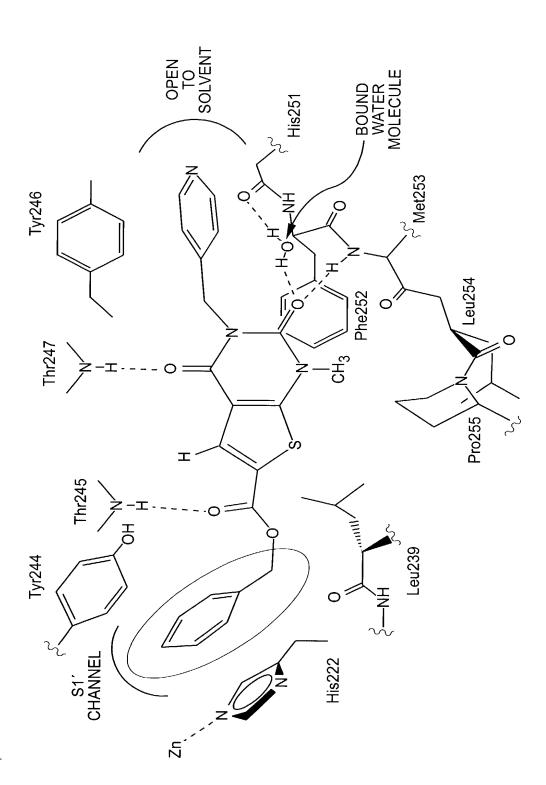
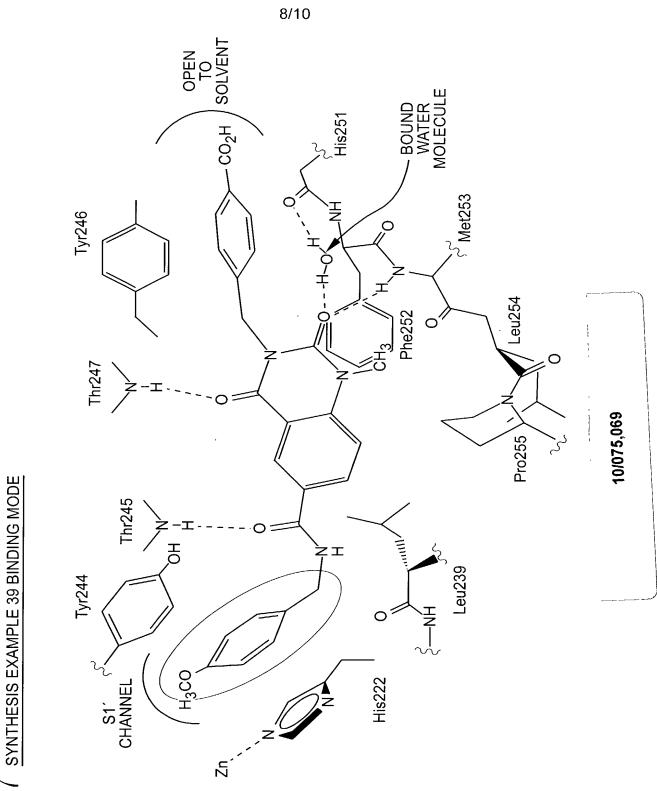


FIG. 6 FUSED BICYCLIC PYRIMIDONES-BINDING MODE



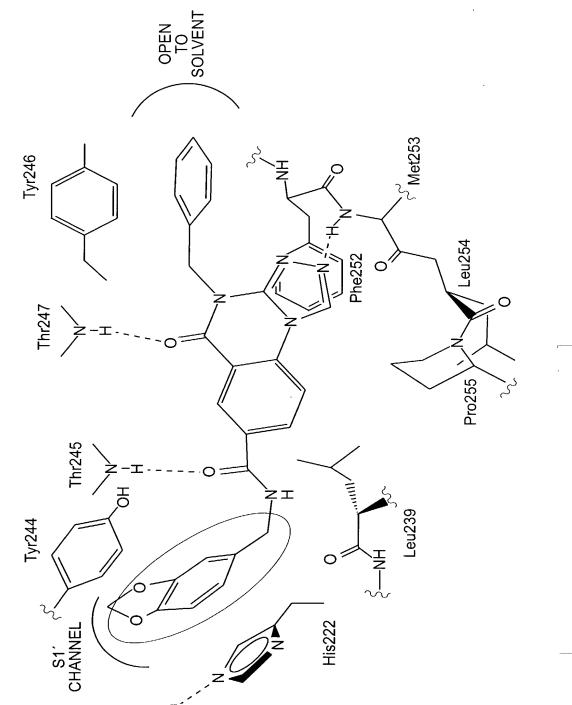


FIG. 8 SYNTHESIS EXAMPLE 57 BINDING MODE

10/10

9.07, 0, 0/ 7.15, 0.80, 0 ပ 6.4 4.6 5 5.08, 2.23, 0 52 1.0 5.5 10.4 -140 0, 0, 0 A -1.52, -3.06, -0.23 3.4 ₩ □ LSPLANE1

. 9 COORDONATES IN THE SPACE OF THE HYDROPHOBIC GROUPS AND HYDROGEN BOND ACCEPTORS OF THE PHARMACOPHORE